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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary

Application No.

10/519,390

Applicant(s)

CHUNG ET AL.

Examiner

CHERIE M. WOODWARD

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 18 September 2007.
2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 38, 40-42, 62 and 75 is/are pending in the application.
4a) Of the above claim(s) _____ is/are withdrawn from consideration.
5) ☐ Claim(s) _____ is/are allowed.
6) ☒ Claim(s) 38, 40-42, 62, and 75 is/are rejected.
7) ☐ Claim(s) _____ is/are objected to.
8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SF/08)
Paper No(s)/Mail Date _____
4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date _____
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____

DETAILED ACTION

Formal Matters

1. Applicant's Response and Amendments to the claims and the specification, filed 28 May 2007 and 18 September 2007, are acknowledged and entered. Claims 1-37, 39, 43-61, and 63-74 have been cancelled by Applicant. New claim 75 has been added. Claims 38, 40-42, 62, and 75 are pending and under examination.

Response to Arguments

Specification – Objections

2. The objection regarding the use of trademarks is withdrawn in light of Applicant's amendments to the specification.
3. The objection to the title of the invention is maintained for the reasons of record, but will be held in abeyance. Applicant has indicated that the title will be changed when allowable subject matter is identified (see Remarks, filed 28 May 2007, p. 9 of 13).

Claim Rejections Withdrawn

4. Rejections over cancelled claim 39 are withdrawn as moot in light of Applicant's cancellation of claim 39.
5. The rejection of claims 38, 40-42, and 62 under 35 U.S.C. 112, first paragraph, scope of enablement, is withdrawn, in light of Applicant's amendments.
6. The rejection of claims 41, 42 and 62 under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement, is withdrawn in light of Applicant's amendments.
7. The rejection of claims 38, 40-42 and 62 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention, regarding the phrase "of an amino acid sequence designated as SEQ ID NO: 25" is withdrawn in light of Applicant's amendments.

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8. The rejection of claim 38 under 35 U.S.C. 102(b) as being anticipated by Smulevich et al., (Biochemistry 1994; 33(23):7398-7407), is withdrawn in light of Applicant's amendments.

Claim Rejections Maintained

Claim Rejections - 35 USC § 112, First Paragraph

Written Description

9. Claims 38 and 40 remain rejected and new claim 75 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement.

Applicant argues that the examiner lacks experimental evidence to substantiate her argument that it would require undue experimentation to extrapolate a F-V substitution to any cytokine binding domain (Remarks, page 12). Applicant argues that undue experimentation would not be required to make variants within the scope of the claims (Remarks, page 12), but rather that the experimentation would be nothing more than routine experimentation (Remarks, page 13). Applicant agrees with the Examiner that an F-V substitution would be labor intensive, but argues that the work necessary to make the genus of claimed cytokine binding domain variants would not require undue experimentation (Remarks, page 13).

Applicant's arguments have been fully considered, but they are not persuasive.

Applicant confuses the requirements of written description under 35 USC 112, first paragraph, with the requirements for enablement under 35 USC 112, first paragraph. The enablement requirement states that Applicant must provide support and guidance in the specification so as to permit one of skill in the art to make and use the claimed invention without undue experimentation. The written description requirement states that Applicant must adequately describe the claimed invention such that one of skill in the art would understand that Applicant was in possession of the invention, as claimed, at the time the application was filed. In Applicant's response, the only argument found that is directed to possession of the invention, as claimed, is found at page 12, first paragraph. Applicant's arguments, while appearing to be directed to the written description rejection, do not rebut the examiner's assertions that Applicant was not in possession of the genus of protein variants, as claimed. Applicant is strongly encouraged to review the USPTO Guidelines for the Examination of Patent Applications under 35 USC 112, paragraph 1, "Written Description."

Vas-Cath Inc. v. Mahurkar, 935 F.2d 1555, 1563-64, 19 USPQ2d 1111, 1117 (Fed. Cir. 1991) states that Applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. *Vas-Cath, Inc. v. Mahurkar*, makes clear that the written description provision of 35 U.S.C. 112 is severable from its enablement provision (see p.

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1115). The invention, for purposes of the written description inquiry, is whatever is now claimed (see page 1117).

In this case, Applicant's claims are drawn to a broad genus of protein variants having a F-V mutation in a binding domain of a cytokine (claim 38), wherein the cytokine is a 4-alpha helix bundle cytokine (claim 40). Neither these claims nor the specification adequately describe F-V mutations in the genus of claimed variants such that one of skill in the art would be aware that Applicant was in possession of the entire genus of protein variants at the time the instant application was filed. The disclosure of a single disclosed species may provide an adequate written description of a genus when the species disclosed is representative of the genus. However, the present claim encompasses numerous species that are not further described. Applicant's claims do not reasonably correlate with the description of cytokine binding domain variants as set forth in the specification.

The state of the art demonstrates that the structures and sequences of most cytokines are known or have been proposed. As such, one of skill in the art would reasonably be able to determine which proteins are cytokines and where their binding domains are located. The instant specification sets forth a non-limiting list of cytokines on pages 7 and 8. The specification also recites SEQ ID NOs for the proteins recited in claim 41 (see pp. 18-20). Table 3 (p. 40) exemplifies G-CSF F-V variants, Table 5 (p. 42) exemplifies GH (growth hormone) F-V variants, and Table 6 (p. 48) exemplifies IGF-1 variants. EPO and TPO variants are taught throughout, especially at Tables 1 (p. 37), 2 (p. 39), 7 and 8 (p. 51), 9 and 10 (p. 54) and 11 (p. 56) (see also Examples 5 and 8, pp. 48-51 and 56). Example 8 (p. 53) also demonstrates the biological activities of TPO, EPO, G-CSF, and GH muteins. These protein variants are adequately described in terms of both their structure and function with regard to their biological activities. While "examples explicitly covering the full scope of the claim language" typically will not be required, a sufficient number of representative species must be included to "demonstrate that the patentee possessed the full scope of the [claimed] invention." *Lizardtech v. Earth Resource Mapping, Inc.*, 424 F.3d 1336, 1345, 76 USPQ2d 1724, 1732 (Fed. Cir. 2005).

Applicant has only described the structure and biological function of cytokine binding domain variants for TPO, EPO, G-CSF, GH, and IGF-1. For example, although the structure of the interleukins recited in claims 41 and 42 are set forth in the specification and are known in the art, no examples are provided such that one of skill in the art would be aware that Applicant was in possession of the species of interleukin variants in claims 41 and 42, such that Applicant has set forth a sufficient number of species that would be representative of the genus of interleukins and by extension, the genus 4-alpha helix

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bundle cytokines (claim 40) and the broader genus of cytokines (claim 38). The description of the species of TPO, EPO, GH, G-CSF, and IGF-1 is not sufficient to satisfy the breadth of broader claims 38 and 40.

Applicant argues that one of skill in the art may "extrapolate" the F-V substitutions to any cytokine by following the examples of the species of cytokines set forth in the specification. The Univ. of Rochester v. G.D. Searle & Co., (358 F.3d 916, 927, 69 USPQ2d 1886, 1895 (Fed. Cir. 2004)) and Ex Parte Kubin, (2007-0819, BPAI 31 May 2007, opinion at p. 16, paragraph 1) opinions explicitly state that possession may not be shown by merely describing how to obtain possession of members of the claimed genus or how to identify their common structural features.

New claim 75 is rejected because it recites a pharmaceutical composition comprising the protein variant of claims 38 or 40 in the alternative and a pharmaceutically acceptable carrier.

In the absence of sufficient recitation of distinguishing characteristics, the specification does not provide adequate written description of the claimed genus of claims 38 and 40, which are protein variants which substitute a valine residue for a phenylalanine residue in a binding domain of a cytokine, wherein the cytokine is a 4-alpha helix bundle cytokine. One of skill in the art would not recognize from the disclosure that the applicant was in possession of the genus of cytokine binding domain mutants, as claimed.

Claim Rejections - 35 USC § 112, Second Paragraph

10. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

11. Claims 38, 40-42 remain rejected and new claim 75 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention, for the reasons of record and the reasons set forth herein,

Applicant argues that the amendment to claim 62 has obviated the rejection. Applicant's arguments have been fully considered, but they are not persuasive as to claims 38, 40, 42, or 75.

Claim 42 recites the protein variant of claim 41 (which is subsequently dependent on claims 40 and 38) wherein the member of the recited group is altered by substituting valine for phenylalanine between positions 110 and 180. The phrase "residue of amino acid residues between positions 110 and 180" does not set forth whether these residues are to be determined from the sequence of the wild-type protein with its signal sequence or from the mature protein (the protein without its signal sequence). Most signal sequences in cytokines are 15-25 residues in length and the starting point from which to

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calculate residues 110-180 must be clear, otherwise the reference points of 110-180 are unclear and confusing. Applicant should compare claim 62 (which is not included in this rejection). Claim 62 sets forth a SEQ ID number that clearly sets forth the starting point (i.e. residue number 1) such that one may more clearly determine the residues that fall between positions 110 and 180. It is noted that the specification recites SEQ ID NOs for the proteins recited in claim 41 (see pp. 18-20). The claims may be read in light of the specification, but the limitations of the specification may not be read into the claims. If it is Applicant's intention that the protein variants be recognized in view of their SEQ ID NO, so as to more clearly ascertain the starting point of residue 1, then Applicant should clarify the claims to reflect this association.

New Claim Rejections – Necessitated by Amendment

Claim Rejections - 35 USC § 102

12. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

13. Claims 38, 40-42, 62, and 75 are rejected under 35 U.S.C. 102(e) as being anticipated by Roberts et al., US Pregrant Publication 20050220800 (published 24 August 2005, benefit to 1 May 2002).

The amended claims recite a protein variant which substitutes a valine residue for a phenylalanine residue in a binding domain of a cytokine; wherein the cytokine is a 4-alpha helix bundle cytokine; wherein the 4-alpha helix bundle is selected from the recited group comprising TPO, wherein the F-V substitution occurs between residues 110 and 180; wherein the substitution in TPO is at F141V.

Roberts et al., teach TPO variant F141V at paragraph 160 (see also Figure 9). A composition comprising the protein is taught at paragraph 24 and claim 31.

Conclusion

NO CLAIM IS ALLOWED.

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14. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to CHERIE M. WOODWARD whose telephone number is (571)272-3329. The examiner can normally be reached on Monday - Friday 9:00am-5:30pm (EST).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Manjunath N. Rao can be reached on (571) 272-0939. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/CMW/

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/Manjunath N. Rao, /

Supervisory Patent Examiner, Art Unit 1647